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January 20, 2006

WRITER'S DIRECT NUMBER:
(202) 772-8606
INTERNET ADDRESS:
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Attn: Mail Stop Amendment

Re: U.S. Utility Patent Application
Application No. 10/698,924; Filed: October 31, 2003
For: **Novel Cyclic Phosphate Diesters of 1,3-Propane-1-Aryl Diols and
Their Use in Preparing Prodrugs**
Inventors: REDDY *et al.*
Our Ref: 2358.0180003/RWE/AES

Sir:

Transmitted herewith for appropriate action are the following documents:

1. Credit Card Payment Form (PTO-2038) in the amount of **\$180.00** to cover Information Disclosure Statement Filing fee (37 C.F.R. § 1.17(p));
2. Second Supplemental Information Disclosure Statement Filing Under 37 C.F.R. § 1.97(c);
3. One (1) page of Form PTO/SB/08A citing nineteen (19) documents;
4. Copies of nine (9) of the cited documents (Documents AN-AV);
5. Ten (10) pages of Form PTO/SB/08B citing one hundred four (104) documents;
6. Copies of the one hundred four (104) cited documents (Document AW-EV); and
7. One (1) return postcard.

It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier. In the event that extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned.

Commissioner for Patents
January 20, 2006
Page 2

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Ann E. Summerfield
Attorney for Applicants
Registration No. 47,982

AES/law
Enclosures

487560_1.DOC



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Reddy *et al.*

Appl. No.: 10/698,924

Filed: October 31, 2003

For: **Novel Cyclic Phosphate Diesters of
1,3-Propane-1-Aryl Diols and
Their Use In Preparing Prodrugs**

Confirmation No.: 2985

Art Unit: 1626

Examiner: Taofiq A. Solola

Atty. Docket: 2358.0180003/RWE/AES

**Second Supplemental Information Disclosure Statement
Filing Under 37 C.F.R. § 1.97(c)**

Mail Stop Amendment

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Sir:

Listed on accompanying Forms PTO/SB/08A and PTO/SB/08B are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98. The numbering on this Second Supplemental Information Disclosure Statement is a continuation of the numbering in Applicants' First Supplemental Information Disclosure Statement filed on May 24, 2004 in connection with the above-captioned application.

Copies of documents **AN-AV** and **AW-EV** are submitted. However, in accordance with 37 C.F.R. § 1.98(a)(2), copies of U.S. patents and patent application publications, documents **AD-AM**, cited on the attached Form PTO/SB/08A are not submitted.

The Examiner's attention is directed to the following co-pending U.S. Patent Applications, which are directed to related technical subject matter:

Application No. 10/698,928, inventors Boyer, S., *et al.*, filed October 31, 2003, published as US 2004/0092476 A1, cited herein as document **AL**; and

Application No. 11/145,194, inventors Erion, M.D., *et al.*, filed June 3, 2005, published as US 2005/0288240 A1, cited herein as document **AM**.

01/23/2006 HALI11 00000192 10698924

01 FC:1806

180.00 DP

In accordance with the recent Federal Circuit decision in *Dayco Prods., Inc. v. Total Containment, Inc.* 329 F.3d 1358 (Fed. Cir. 2003), Applicants submit herewith an Office Action, which is directed to related technical subject matter:

Office Action for related U.S. Patent Application No. 10/698,928, inventors Boyer, S., *et al.*, filed October 31, 2003, mailed July 5, 2005, cited herein as document EV.

The identification of these U.S. Patent Applications and Office Action is not to be construed as a waiver of secrecy as to those applications now or upon issuance of the present application as a patent. The Examiner is respectfully requested to consider the cited applications and the art cited therein during examination.

Where the publication date of a listed document does not provide a month of publication, the year of publication of the listed document is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the month of publication is not in issue. Applicants have listed publication dates on the attached IDS Forms based on information presently available to the undersigned. However, the listed publication dates should not be construed as an admission that the information was actually published on the date indicated.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

This statement should not be construed as a representation that a search has been made, or that information more material to the examination of the present patent application does not exist. The Examiner is specifically requested not to rely solely on the material submitted herewith.

This Information Disclosure Statement is being filed more than three months after the U.S. filing date AND after the mailing date of the first Office Action on the merits, but before the mailing date of a Final Rejection, or Notice of Allowance, or an action that otherwise closes prosecution in the application. Attached is our PTO-2038

Credit Card Payment Form in the amount of \$ 180⁰⁰ in payment of the fee under 37 C.F.R. § 1.17(p).

It is respectfully requested that the Examiner initial and return copies of the enclosed IDS Forms, and indicate in the official file wrapper of this patent application that the documents have been considered.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Ann E. Summerfield
Attorney for Applicants
Registration No. 47,982

Date: January 20, 2006

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Equivalent of Form PTO/SB/08A (07-05)

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Substitute for form 1449/PTO

**SECOND SUPPLEMENTAL
INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Complete if Known

Application Number	10/698,924
Filing Date	October 31, 2003
First Named Inventor	K. Raja Reddy
Art Unit	1626
Examiner Name	Taofiq A. Solola
Attorney Docket Number	2358.0180003/RWE/AES

Sheet 1 of 1

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	AD	3,018,302	01/23/1962	Bielefeld <i>et al.</i>	
	AE	3,116,282	12/31/1963	Hunter	
	AF	4,440,740	04/03/1984	Fix <i>et al.</i>	
	AG	4,952,740	08/28/1990	Juge <i>et al.</i>	
	AH	5,663,159	09/02/1997	Starrett Jr., <i>et al.</i>	
	AI	6,752,981	06/22/2004	Erion <i>et al.</i>	
	AJ	2003/0229225 A1	12/11/2003	Reddy <i>et al.</i>	
	AK	2003/0225277 A1	12/04/2003	Kopcho <i>et al.</i>	
	AL	2004/0092476 A1	05/13/2004	Erion <i>et al.</i>	
	AM	2005/0288240 A1	12/29/2005	Erion <i>et al.</i>	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ Number ⁴ Kind Code ⁵ (if known)				
	AN	EP 0161955 A1	11/21/1985	Merck & Co., Inc.		
	AO	EP 0180276 A1	05/07/1986	Oce-Andeno B.V.		
	AP	EP 0338372 A2	10/25/1989	American Cyanamid Co.		
	AQ	EP 0353692 B1	10/04/1995	Nissan Chemical Ind., Ltd.		
	AR	EP 0481214 B1	06/24/1998	Inst. Organic Chem. & Biochem. Acad. Sci. Czech. Repub.		
	AS	WO 91/19721 A1	12/26/1991	Glazier		
	AT	WO 96/01267 A1	01/18/1996	Takeda Chemical Ind., Ltd.		
	AU	WO 97/03679 A1	02/06/1997	Cephalon, Inc.		
	AV	WO 00/52015 A2	09/08/2000	Metabasis Therapeutics, Inc.		

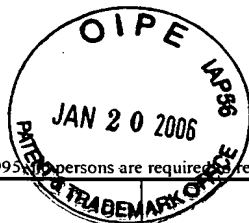
484547_1.DOC

Examiner Signature	Date Considered
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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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PTO/SB/08B (07-05)

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Substitute for form 1449/PTO				Complete if Known	
SECOND SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)				Application Number	10/698,924
				Filing Date	October 31, 2003
				First Named Inventor	K. Raja Reddy
				Art Unit	1626
				Examiner Name	Taofiq A. Solola
Sheet	1	of	10	Attorney Docket Number	2358.0180003/RWE/AES

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume issue number(s), publisher, city and/or country where published	T ²
	AW	ALEXANDER, P., <i>et al.</i> , "Preparation of 9-(2-Phosphonomethoxyethyl) Adenine Esters as Potential Prodrugs," <i>Collect. Czech. Chem. Commun.</i> 59:1853-1869, Czech Academy of Sciences, Institute of Organic Chemistry and Biochemistry (1994)	
	AX	AMIN, D., <i>et al.</i> , "1-Hydroxy-3-(methylpentylamino)-propylidene-1,1-bisphosphonic Acid as a Potent Inhibitor of Squalene Synthase," <i>Arzneim.-Forsch/Drug Res.</i> 46:759-762, Blackwell Publishing, Inc. (1996)	
	AY	ARNÉR, E.S.J. and ERIKSSON, S., "Mammalian Deoxyribonucleoside Kinases," <i>Pharmacol. Ther.</i> 67:155-186, Elsevier Science Ltd. (1995)	
	AZ	ATIQ, O., <i>et al.</i> , "Treatment of Unresectable Primary Liver Cancer with Intrahepatic Fluorodeoxyuridine and Mitomycin C Through an Implantable Pump," <i>Cancer</i> 69:920-924, John Wiley and Sons, Inc. (1992)	
	BA	AUBERSON, Y., <i>et al.</i> , "N-Phosphonoalkyl-5-Aminomethylquinoxaline-2,3-Diones: <i>In Vivo</i> Active AMPA and NMDA-(Glycine) Antagonists," <i>Bioorg. Med. Chem. Lett.</i> 9:249-254, Elsevier Science Ltd. (1999)	
	BB	BALTHAZOR, T. and Grabiak, R.C., "Nickel-Catalyzed Arbuzov Reaction: Mechanistic Observations," <i>J. Org. Chem.</i> 45:5425-5426, American Chemical Society (1980)	
	BC	BEAUCAGE, S.L. and Iyer, R.P., "The Synthesis of Modified Oligonucleotides by the Phosphoramidite Approach and Their Applications," <i>Tetrahedron</i> 49:6123-6194, Pergamon Press Ltd. (1993)	
	BD	BESPALOV, A., <i>et al.</i> , "Prolongation of morphine analgesia by competitive NMDA receptor antagonist D-CPPene (SDZ EAA 494) in rats," <i>Eur. J. Pharmacol.</i> 351:299-305, Elsevier Science B.V. (1998)	
	BE	BIRD, J., <i>et al.</i> , "Synthesis of Novel N-Phosphonoalkyl Dipeptide Inhibitors of Human Collagenase," <i>J. Med. Chem.</i> 37:158-169, American Chemical Society (1994)	
	BF	BORCH, R.F. and Millard, J.A., "The Mechanism of Activation of 4-Hydroxycyclophosphamide," <i>J. Med. Chem.</i> 30:427-431, American Chemical Society (1987)	

Examiner Signature		Date Considered	
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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

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Substitute for form 1449/PTO SECOND SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(Use as many sheets as necessary)</i>				Complete if Known	
				Application Number	10/698,924
				Filing Date	October 31, 2003
				First Named Inventor	K. Raja Reddy
				Art Unit	1626
				Examiner Name	Taofiq A. Solola
Sheet	2	of	10	Attorney Docket Number	2358.0180003/RWE/AES

	BG	BRILL, T. and Landon, S.J., "Arbuzov-like Dealkylation Reactions of Transition-Metal-Phosphite Complexes," <i>Chem. Rev.</i> 84:577-585, American Chemical Society (1984)	
	BH	CAMPAGNE, J.-M., <i>et al.</i> , "Synthesis of Mixed Phosphate Diester Analogues of Dipeptides using BOP or PyBOP Reagents," <i>Tetrahedron Lett.</i> 34:6743-6744, Pergamon Press Ltd. (1993)	
	BI	CAMPBELL, D.A., "The Synthesis of Phosphonate Esters, an Extension of the Mitsunobu Reaction," <i>J. Org. Chem.</i> 57:6331-6335, American Chemical Society (1992)	
	BJ	CASARA, P., <i>et al.</i> , "Synthesis of Acid Stable 5'-O-Fluoromethyl Phosphonates of Nucleosides. Evaluation as Inhibitors of Reverse Transcriptase," <i>Bioorg. Med. Chem. Lett.</i> 2:145-148, Pergamon Press plc (1992)	
	BK	CASTEEL, D. and Peri, S.P., "Steric and Electronic Effects in the Aryl Phosphate to Arylphosphonate Rearrangement," <i>Synthesis</i> (9):691-693, Georg Thieme Verlag KG (1991)	
	BL	CHEN, L. and Waxman, D.J., "Intratumoral Activation and Enhanced Chemotherapeutic Effect of Oxazaphosphorines following Cytochrome P-450 Gene Transfer: Development of a Combined Chemotherapy/Cancer Gene Therapy Strategy," <i>Cancer Res.</i> 55:581-589, The American Association for Cancer Research (1995)	
	BM	CHEN, L., <i>et al.</i> , "Sensitization of Human Breast Cancer Cells to Cyclophosphamide and Ifosfamide by Transfer of a Liver Cytochrome P450 Gene," <i>Cancer Res.</i> 56:1331-1340, The American Association for Cancer Research (1996)	
	BN	COOPER, D.B., <i>et al.</i> , "Use of Carbohydrate Derivatives for Studies of Phosphorus Stereochemistry. Part II. Synthesis and Configurational Assignments of 1,-3,2-Oxathiaphosphorinan-2-ones and 1,3,2-Dioxaphosphorinan-2-thiones," <i>J. Chem. Soc. Perkin I</i> 3/2422:1049-1052, Royal Society of Chemistry (1974)	
	BO	DEARFIELD, K., <i>et al.</i> , "Analysis of the genotoxicity of nine acrylate/methacrylate compounds in L5178Y mouse lymphoma cells," <i>Mutagenesis</i> 4:381-393, Oxford University Press (1989)	
	BP	DE CLERCQ, E., <i>et al.</i> , "A novel selective broad-spectrum anti-DNA virus agent," <i>Nature</i> 323:464-467, Nature Publishing Group (1986)	
	BQ	DE LOMBAERT, S., <i>et al.</i> , "Pharmacological Profile of a Non-Peptidic Dual Inhibitor of Neutral Endopeptidase 24.11 and Endothelin-Converting Enzyme," <i>Biochem. Biophys. Res. Commun.</i> 204:407-412, Academic Press, Inc. (1994)	

Examiner Signature		Date Considered	
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SECOND SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)				Application Number	10/698,924
				Filing Date	October 31, 2003
				First Named Inventor	K. Raja Reddy
				Art Unit	1626
				Examiner Name	Taofiq A. Solola
Sheet	3	of	10	Attorney Docket Number	2358.0180003/RWE/AES
	BR	DE LOMBAERT, S., <i>et al.</i> , "N-Phosphonomethyl Dipeptides and Their Phosphonate Prodrugs, a New Generation of Neutral Endopeptidase (NEP, EC 3.4.24.11) Inhibitors," <i>J. Med. Chem.</i> 37:498-511, American Chemical Society (1994)			
	BS	DESOS, P., <i>et al.</i> , "Structure-Activity Relationships in a Series of 2(1 <i>H</i>)-Quinolones Bearing Different Acidic Function in the 3-Position: 6,7-Dichloro-2(1 <i>H</i>)-oxoquinoline-3-phosphonic Acid, a New Potent and Selective AMPA/Kainate Antagonist with Neuroprotective Properties," <i>J. Med. Chem.</i> 39:197-206, American Chemical Society (1996)			
	BT	DE WAZIERS, <i>et al.</i> , "Cytochrome P450 Isoenzymes, Epoxide Hydrolase and Glutathione Transferases in Rat and Human Hepatic and Extrahepatic Tissues," <i>J. Pharm. Exp. Ther.</i> 253:387-394, American Society for Pharmacology and Experimental Therapeutics (1990)			
	BU	DICKSON, J.K., <i>et al.</i> , "Orally Active Squalene Synthase Inhibitors: Bis((acyloxy)alkyl) Prodrugs of the α -Phosphonosulfonic Acid Moiety," <i>J. Med. Chem.</i> 39:661-664, American Chemical Society (1996)			
	BV	ENRIQUEZ, P., <i>et al.</i> , "Conjugation of Adenine Arabinoside 5'-Monophosphate to Arabinogalactan: Synthesis, Characterization, and Antiviral Activity," <i>Bioconjugate Chem.</i> 6:195-202, American Chemical Society (1995)			
	BW	ERION, M., <i>et al.</i> , "Design, Synthesis, and Characterization of a Series of Cytochrome P ₄₅₀ 3A-Activated Prodrugs (HepDirect Prodrugs) Useful for Targeting Phosph(on)ate-Based Drugs to the Liver," <i>J. Am. Chem. Soc.</i> 126:5154-5163, American Chemical Society (April 2004)			
	BX	ERION, M., <i>et al.</i> , "HepDirect™ Prodrugs: A Novel Strategy for Targeting Drugs to the Liver," <i>Hepatology</i> 36:301A, AASLD Abstract No. 551, John Wiley & Sons, Inc. (October 2002)			
	BY	ERION, M., <i>et al.</i> , "Liver-Targeted Drug Delivery Using HepDirect Prodrugs" <i>J. Pharmacol. Exper. Ther.</i> 312:554-560, American Society for Pharmacology and Experimental Therapeutics (February 2005)			
	BZ	ERION, M., "Liver-Targeted Nucleoside Prodrugs," presented at the <i>Gordon Research Conference: Purines, Pyrimidines and Related Substances</i> , Newport, RI, 38 pages (June-July 2003)			
	CA	FARQUHAR, D., <i>et al.</i> , "Biologically-Cleavable Phosphate Protective Groups: 4-Acyloxy-1,3,2-Dioxaphosphorinanes as Neutral Latent Precursors of Dianionic Phosphates," <i>Tetrahedron Lett.</i> 36:655-658, Elsevier Science Ltd. (1995)			
	CB	FARQUHAR, D., <i>et al.</i> , "Biologically Reversible Phosphate-Protective Groups," <i>J. Pharm. Sci.</i> 72:324-325, American Chemical Society (1983)			

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				Filing Date	October 31, 2003
				First Named Inventor	K. Raja Reddy
				Art Unit	1626
				Examiner Name	Taofiq A. Solola
				Attorney Docket Number	2358.0180003/RWE/AES
Sheet	4	of	10		

	CC	FARQUHAR, D., <i>et al.</i> , "Synthesis and Antitumor Evaluation of Bis[(pivaloyloxy) methyl] 2'-Deoxy-5-fluorouridine 5'-Monophosphate (FdUMP): A Strategy to Introduce Nucleotides into Cells," <i>J. Med. Chem.</i> 37:3902-3909, American Chemical Society (1994)	
	CD	FARQUHAR, D., <i>et al.</i> , Synthesis and Biological Evaluation of 9-[5'-(2-Oxo-1,3,2-oxazaphosphorinan-2-yl)-β-D-arabinosyl]adenine and 9-[5'-(2-Oxo-1,3,2-dioxaphosphorinan-2-yl)-β-D-arabinosyl]adenine: Potential Neutral Precursors of 9-[β-D-Arabinofuranosyl]adenine 5'-Monophosphate," <i>J. Med. Chem.</i> 28:1358-1361, American Chemical Society (1985)	
	CE	FARQUHAR, D., <i>et al.</i> , "5'-4-(Pivaloyloxy)-1,3,2-dioxaphosphorinan-2-yl]-2'-deoxy-5-fluorouridine: A Membrane-Permeating Prodrug of 5-Fluoro-2'-deoxyuridylic Acid (FdUMP)," <i>J. Med. Chem.</i> 38, 488-495, American Chemical Society (1995)	
	CF	FARQUHAR, D., <i>et al.</i> , "Synthesis and Biological Evaluation of Neutral Derivatives of 5-Fluoro-2'-deoxyuridine 5'-Phosphate," <i>J. Med. Chem.</i> 26:1153-1158, American Chemical Society (1983)	
	CG	FIUME, L., <i>et al.</i> , "Inhibition of Hepatitis B Virus Replication by Vidarabine Monophosphate Conjugated with Lactosaminated Serum Albumin," <i>The Lancet</i> 2:13-15, The Lancet Publishing Group (1988)	
	CH	FREED, J.J., <i>et al.</i> , "Evidence for Acyloxymethyl Esters of Pyrimidine, 5'-Deoxyribonucleotides as Extracellular Sources of Active 5'-Deoxyribonucleotides in Cultured Cells," <i>Biochem. Pharm.</i> 38:3193-3198, Elsevier Inc. (1989)	
	CI	FRIIS, G.J. and Bundgaard, H., "Prodrugs of phosphates and phosphonates: Novel lipophilic α-acyloxyalkyl ester derivatives of phosphate- or phosphonate containing drugs masking the negative charges of these groups," <i>Eur. J. Pharm. Sci.</i> 4:49-59, Elsevier Science B.V. (1996)	
	CJ	FUJII, A., <i>et al.</i> , "Ruthenium(II)-Catalyzed Asymmetric Transfer Hydrogenation of Ketones Using a Formic Acid-Triethylamine Mixture," <i>J. Am. Chem. Soc.</i> 118:2521-2522, American Chemical Society (1996)	
	CK	GUIDA, W.C., <i>et al.</i> , "Structure-Based Design of Inhibitors of Purine Nucleoside Phosphorylase. 4. A Study of Phosphate Mimics," <i>J. Med. Chem.</i> 37:1109-1114, American Chemical Society (1994)	
	CL	HE, K., <i>et al.</i> , "Inactivation of Cytochrome P450 3A4 by Bergamottin, a Component of Grapefruit Juice," <i>Chem. Res. Toxicol.</i> 11:252-259, American Chemical Society (1998)	
	CM	HESSLER, "An Efficient Synthesis of 1-β-D-Arabinofuranosylcytosine," <i>J. Org. Chem.</i> 41:1828-1831 (1976)	

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				Application Number	10/698,924
				Filing Date	October 31, 2003
				First Named Inventor	K. Raja Reddy
				Art Unit	1626
				Examiner Name	Taofiq A. Solola
Sheet 5 of 10				Attorney Docket Number	2358.0180003/RWE/AES
	CN	HILLERS, S., <i>et al.</i> , "Analogues of pyrimidinemono- and polynucleotides. VI. Phosphates of 1-(1,4-dihydroxy-2-pentyl)thymine and 1-(1,3-dihydroxy-2-propyl) uracil," <i>Chemical Abstracts</i> 89(17), Chemical Abstracts Service (1978)			
	CO	HIRAYAMA, N., <i>et al.</i> , "Structure and conformation of a novel inhibitor of angiotensin I converting enzyme - a tripeptide containing phosphonic acid," <i>Int. J. Pept. Protein Res.</i> 38:20-24, Blackwell Publishing (1991)			
	CP	HUNSTON, R., <i>et al.</i> , "Synthesis and Biological Properties of Some Cyclic Phosphotriesters Derived from 2'-Deoxy-5-fluorouridine," <i>J. Med. Chem.</i> 27:440-444, American Chemical Society (1984)			
	CQ	KEENAN, R., <i>et al.</i> , "Pathology Reevaluation of the Kociba <i>et al.</i> (1978) Bioassay of 2,3,7,8-TCDD: Implications for Risk Assessment," <i>J. Tox. Envir. Health</i> 34:279-296, Hemisphere Publishing Corporation (1991)			
	CR	KELLEY, J.L., <i>et al.</i> , "[[(Guaninylalkyl)phosphinico]methyl]phosphonic Acids. Multisubstrate Analogue Inhibitors of Human Erythrocyte Purine Nucleoside Phosphorylase," <i>J. Med. Chem.</i> 38:1005-1014, American Chemical Society (1995)			
	CS	KHAMNEI, S. and Torrence, P.F., "Neighboring Group Catalysis in the Design of Nucleotide Prodrugs," <i>J. Med. Chem.</i> 39:4109-4115, American Chemical Society (1996)			
	CT	KHORANA, H.G., <i>et al.</i> , "Cyclic Phosphates. III. Some General Observations on the Formation of Properties of Five-, Six- and Seven-membered Cyclic Phosphate Esters," <i>J. Am. Chem. Soc.</i> 79:430-436, American Chemical Society (1957)			
	CU	KORBA, B.A., <i>et al.</i> , "Liver-Targeted Antiviral Nucleosides: Enhanced Antiviral Activity of Phosphatidyl-Dideoxyguanosine Versus Dideoxyguanosine in Woodchuck Hepatitis Virus Infection <i>In Vivo</i> ," <i>Hepatology</i> 23:958-963, John Wiley & Sons, Inc. (1996)			
	CV	KRYUCHKOV, A.A., <i>et al.</i> , "Influence of Solvent on the Strength of Cyclic Oxygen-Containing Phosphorus Acids," <i>Bull. Acad. Sci. USSR, A translation of Izvestiya Akademii Nauk SSSR, Ser. Khim.</i> 36:1145-1148, Consultants Bureau (1987)			
	CW	LEFEBVRE, I., <i>et al.</i> , "Mononucleoside Phosphotriester Derivatives with S-Acyl-2-thioethyl Bioreversible Phosphate-Protecting Groups: Intracellular Delivery of 3'-Azido-2',3'-dideoxythymidine 5'-Monophosphate," <i>J. Med. Chem.</i> 38:3941-3950, American Chemical Society (1995)			
	CX	LOK, A.S.F., <i>et al.</i> , "Neurotoxicity associated with adenine arabinoside monophosphate in the treatment of chronic hepatitis B virus infection," <i>J. Antimicrob. Chemotherap.</i> 14:93-99, Oxford University Press (1984)			

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Substitute for form 1449/PTO				Complete if Known	
SECOND SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(Use as many sheets as necessary)</i>				Application Number	10/698,924
				Filing Date	October 31, 2003
				First Named Inventor	K. Raja Reddy
				Art Unit	1626
				Examiner Name	Taofiq A. Solola
Sheet	6	of	10	Attorney Docket Number	2358.0180003/RWE/AES
	CY	LU, X. and Zhu, J., "Palladium-Catalyzed Reaction of Aryl Polyfluoroalkanesulfonates with O,O-Dialkyl Phosphonates," <i>Synthesis</i> (8):726-727, Georg Thieme Verlag (1987)			
	CZ	LUDEMAN, S.M., <i>et al.</i> , "Synthesis and Antitumor Activity of Cyclophosphamide Analogues. 4. Preparation, Kinetic Studies, and Anticancer Screening of "Phenylketophosphamide" and Similar Compounds Related to the Cyclophosphamide Metabolite Aldophosphamide," <i>J. Med. Chem.</i> 29:716-727, American Chemical Society (1986)			
	DA	MACKENNA, D., <i>et al.</i> , "MB07133: A HepDirect TM Prodrug of Cytarabine Monophosphate for Use in Hepatocellular Carcinoma," <i>Hepatology</i> 38(Suppl. 1):411A, AASLD Abstract No. 524, John Wiley & Sons, Inc. (October 2003)			
	DB	MCGUIGAN, C., <i>et al.</i> , "Intracellular Delivery of Bioactive AZT Nucleotides by Aryl Phosphate Derivatives of AZT," <i>J. Med. Chem.</i> 36:1048-1052, American Chemical Society (1993)			
	DC	MCGUIGAN, C., <i>et al.</i> , "Kinase Bypass: A New Strategy for Anti-HIV Drug Design," <i>Bioorg. Med. Chem. Lett.</i> 3:1207-1210, Pergamon Press Ltd. (1993)			
	DD	MEIER, C., <i>et al.</i> , "Cyclic Saligenyl Phosphotriesters of 2',3'-Dideoxy-2',3'-dideoxythymidine (d4T) - A New Pro-Nucleotide Approach -" <i>Bioorg. Med. Chem. Lett.</i> 7:99-104, Elsevier Science Ltd. (1997)			
	DE	MEIJER, D.K.F. and van der Sluijs, P., "Covalent and Noncovalent Protein Binding of Drugs: Implications for Hepatic Clearance, Storage, and Cell-Specific Drug Delivery," <i>Pharm. Res.</i> 6:105-118, Plenum Publishing Corporation (1989)			
	DF	MELVIN, L.S., "An Efficient Synthesis of 2-Hydroxyphenylphosphonates" <i>Tetrahedron Lett.</i> 22:3375-3376, Pergamon Press Ltd. (1981)			
	DG	MEYER, R., <i>et al.</i> , "2'-O-Acyl-6-thioinosine Cyclic 3',5'-Phosphates as Prodrugs of Thioinosinic Acid," <i>J. Med. Chem.</i> 22:811-815, American Chemical Society (1979)			
	DH	MITCHELL, A., <i>et al.</i> , "Bioreversible Protection for the Phospho Group: Bioactivation of the Di(4-acyloxybenzyl) and Mono(4-acyloxybenzyl) Phosphoesters of Methylphosphonate and Phosphonacetate," <i>J. Chem. Soc. Perkin Trans. 1</i> , 2345-2353, Royal Society of Chemistry (1992)			
	DI	MITSUNOBU, O., "The Use of Diethyl Azodicarboxylate and Triphenylphosphine in Synthesis and Transformation of Natural Products," <i>Synthesis</i> (1):1-28, Georg Thieme Verlag (1981)			

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				Application Number	10/698,924
				Filing Date	October 31, 2003
				First Named Inventor	K. Raja Reddy
				Art Unit	1626
				Examiner Name	Taofiq A. Solola
Sheet	7	of	10	Attorney Docket Number	2358.0180003/RWE/AES
	DJ	MONTAG, A., <i>et al.</i> , "The Effect of Dexamethasone Treatment on CYP3A Activity Distribution, the Liver Targeting of MB07133 and CYP3A Activity in a Highly Proliferating State in Rats," <i>Hepatology</i> 40(Suppl. 1):649A, AASLD Abstract No. 1123, John Wiley & Sons, Inc. (2004)			
	DK	MOORE, M., <i>et al.</i> , "Comparison of mutagenicity results for nine compounds evaluated at the <i>hprt</i> locus in the standard and suspension CHO assays," <i>Mutagenesis</i> 6:77-85, Oxford University Press (1991)			
	DL	MURRAY, G., <i>et al.</i> , "Cytochrome P450 CYP3A in human renal cell cancer," <i>Brit. J. Cancer</i> 79:1836-1842, Nature Publishing Group (1999)			
	DM	MURRAY, G., <i>et al.</i> , "Cytochrome P450 Expression Is a Common Molecular Event in Soft Tissue Sarcomas," <i>J. Pathology</i> 171:49-52, John Wiley & Sons, Ltd. (1993)			
	DN	NAKAYAMA, K. and Thompson, W.J., "A Highly Enantioselective Synthesis of Phosphate Triesters," <i>J. Am. Chem. Soc.</i> 112:6936-6942, American Chemical Society (1990)			
	DO	NEIDLEIN, R., <i>et al.</i> , "Mild Preparation of 1-Benzoyloxyiminoalkylphosphonic Dichlorides: Application to the Synthesis of Cyclic Phosphonic Diesters and Cyclic Monoester Amides," <i>Heterocycles</i> 35:1185-1203, Elsevier Science (1993)			
	DP	NIFANTYEV, E.E., <i>et al.</i> , "Synthesis and Structure of Some Stable Phospholane-Phospholanes," <i>Phosphorus, Sulfur and Silicon</i> 113:1-13, Overseas Publishers Association (1996)			
	DQ	OGG, M., <i>et al.</i> , "A reporter gene assay to assess the molecular mechanisms of xenobiotic-dependent induction of the human CYP3A4 gene <i>in vitro</i> ," <i>Xenobiotica</i> 29:269-279, Taylor & Francis Ltd. (1999)			
	DR	OHASHI, K., <i>et al.</i> , "Synthesis of Phosphonosphingoglycolipid Found in Marine Snail <u>Turbo Cornutus</u> ," <i>Tetrahedron Lett.</i> 29:1189-1192, Pergamon Press plc (1988)			
	DS	PETRAKIS, K. and Nagabhushan, T.L., "Palladium-Catalyzed Substitutions of Triflates Derived from Tyrosine-Containing Peptides and Simpler Hydroxyarenes Forming 4-(Diethoxyphosphinyl)phenylalanines and Diethyl Arylphosphonates," <i>J. Am. Chem. Soc.</i> 109:2831-2833, American Chemical Society (1987)			
	DT	PITCHER, H.R., "Built-in Bypass," <i>Nature</i> 429:39, Nature Publishing Group (May 2004)			

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				Art Unit	1626
				Examiner Name	Taofiq A. Solola
Sheet	8	of	10	Attorney Docket Number	2358.0180003/RWE/AES
	DU	PREDVODITELEV, D.A., <i>et al.</i> , "Glycero-2-Hydroxymethylene Phosphates," <i>J. Org. Chem. USSR, A Translation of Zhur. Org. Khim.</i> 13:1489-1492, Plenum Publishing Corporation (1977)			
	DV	PREDVODITELEV, D.A., <i>et al.</i> , "Synthesis of Lipids and Their Models on the Basis of Glycerol Alkylene Phosphites. V. Cyclic Phosphatidylglycerol and Phosphatidylhydroxyhomocholine," <i>J. Org. Chem. USSR, A Translation of Zhur. Org. Khim.</i> 17:1156-1165, Plenum Publishing Corporation (1981)			
	DW	REDDY, K.R., <i>et al.</i> , "Stereoselective synthesis of nucleoside monophosphate HepDirect™ prodrugs," <i>Tetrahedron Lett.</i> 46:4321-4324, Elsevier Ltd. (2005)			
	DX	REDDY, M.R., <i>et al.</i> , "Development of a Quantum Mechanics-Based Free-Energy Perturbation Method: Use in the Calculation of Relative Solvation Free Energies," <i>J. Am. Chem. Soc.</i> 126:6224-6225, American Chemical Society (published online April 2004)			
	DY	REDMORE, D., "Phosphorus Derivatives of Nitrogen Heterocycles. 2. Pyridinophosphonic Acid Derivatives," <i>J. Org. Chem.</i> 35:4114-4117, American Chemical Society (1970)			
	DZ	RUIZ VAN HAPEREN, V.W.T., <i>et al.</i> , "Induction of Resistance to 2'-2'-Difluorodeoxycytidine in the Human Ovarian Cancer Cell Line A2780," <i>Semin. Oncol.</i> 22 (Suppl. 1):35-41, W.B. Saunders Company (1995)			
	EA	SHAW, J.-P. and Cundy, K.C., "Biological Screens of PMEA Prodrugs," <i>Pharm. Res.</i> 10:S-294, Kluwer Academic Publishers B.V., Abstract No. PDD 7480 (1993)			
	EB	SHEN, T.Y., <i>et al.</i> , "Nucleosides I. A New Synthesis of 1-β-D-Arabinofuranosyl Pyrimidine Nucleosides," <i>J. Org. Chem.</i> 30:835-838, American Chemical Society (1965)			
	EC	SHIH, Y.-E., <i>et al.</i> , "Preparation and Structures of 2-Dimethylamino-4-phenyl-1,3,2-dioxaphosphorinane-2-oxides," <i>Bull. Inst. Chem. Acad. Sin.</i> 41:9-16, Academia Sinica, Nankang, Taipei, Taiwan (1994)			
	ED	SHIRAI, R., <i>et al.</i> , "Asymmetric Synthesis of Antimitotic Combretadiolane with Potent Antitumor Activity Against Multi-Drug Resistant Cells," <i>Bioorg. Med. Chem. Lett.</i> 8:1997-2000, Elsevier Science Ltd. (1998)			
	EE	STARRETT, Jr., J.E., <i>et al.</i> , "Synthesis, Oral Bioavailability Determination, and <i>in Vitro</i> Evaluation of Prodrugs of the Antiviral Agent 9-[2-(Phosphonomethoxy)ethyl]adenine (PMEA)," <i>J. Med. Chem.</i> 37:1857-1864, American Chemical Society (1994)			

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				Art Unit	1626
				Examiner Name	Taofiq A. Solola
Sheet	9	of	10	Attorney Docket Number	2358.0180003/RWE/AES

	EF	THOMSON, W., <i>et al.</i> , "Synthesis, Bioactivation and Anti-HIV Activity of the Bis(4-acyloxybenzyl) and Mono(4-acyloxybenzyl) Esters of the 5'-monophosphate of AZT," <i>J. Chem. Soc. Perk. Trans.</i> 1,1239-1245, Royal Society of Chemistry (1993)	
	EG	VALENTINE, Jr., D., "Preparation of the Enantiomers of Compounds Containing Chiral Phosphorus Centers," <i>Asymmetric Synthesis</i> 4:263-312, Academic Press, Inc. (1984)	
	EH	VENOOK, A., "Treatment of Hepatocellular Carcinoma: Too Many Options?," <i>J. Clin. Oncol.</i> 12:1323-1334, American Society of Clinical Oncology (1994)	
	EI	VO-QUANG, Y., <i>et al.</i> , "(1-Amino-2-propenyl)phosphonic Acid, an Inhibitor of Alanine Racemase and D-Alanine:D-Alanine Ligase," <i>J. Med. Chem.</i> 29:579-581, American Chemical Society (1986)	
	EJ	WAGNER, A., <i>et al.</i> , "Direct Conversion of Tetrahydropyranylated Alcohols to the Corresponding Bromides," <i>Tetrahedron Lett.</i> 30:557-558, Pergamon Press plc (1989)	
	EK	WALLACE, E.M., <i>et al.</i> , "Design and Synthesis of Potent, Selective Inhibitors of Endothelin-Converting Enzyme," <i>J. Med. Chem.</i> 41:1513-1523, American Chemical Society (1998)	
	EL	WALSH, E., <i>et al.</i> , "Phenoxymethylphosphonic Acids and Phosphonic Acid Ion-exchange Resins," <i>Phenoxymethylphosphonic Acid Ion-Exchange Resins</i> 78:4455-4458, American Chemical Society (1956)	
	EM	WATKINS, P., "Noninvasive tests of CYP3A enzymes," <i>Pharmacogenetics</i> 4:171-184, Lippincott Williams & Wilkins (1994)	
	EN	WEBER, G.F. and Waxman, D.J., "Activation of the Anti-cancer Drug Ifosfamide by Rat Liver Microsomal P450 Enzymes," <i>Biochem. Pharm.</i> 45:1685-1694, Pergamon Press Ltd. (1993)	
	EO	WECHTER, W.J., <i>et al.</i> , "Nucleic Acids. 16. Orally Active Derivatives of ara-Cytidine ^{1,2} ," <i>J. Med. Chem.</i> 19:1013-1017, American Chemical Society (1976)	
	EP	WEIBEL, M., <i>et al.</i> , "Potentiating Effect of {2-[2-[(2-Amino-1,6-Dihydro-6-Oxo-9H-Purin-9-yl)Methyl]-Phenyl] Ethenyl}-Phosphonic Acid (MDL 74,428), A Potent Inhibitor of Purine Nucleoside Phosphorylase, on the Antiretroviral Activities of 2',3'-Dideoxyinosine Combined to Ribavirin in Mice," <i>Biochem. Pharmacol.</i> 48:245-252, Elsevier Science Ltd. (1994)	

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Substitute for form 1449/PTO SECOND SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(Use as many sheets as necessary)</i>				Complete if Known	
				Application Number	10/698,924
				Filing Date	October 31, 2003
				First Named Inventor	K. Raja Reddy
				Art Unit	1626
				Examiner Name	Taofiq A. Solola
Sheet 10 of 10				Attorney Docket Number	2358.0180003/RWE/AES
	EQ	WILEMAN, T., <i>et al.</i> , "Receptor-mediated endocytosis," <i>Biochem. J.</i> 232:1-14, Portland Press (1985)			
	ER	YU, L. J., <i>et al.</i> , "In vivo Modulation of Alternative Pathways of P-450-Catalyzed Cyclophosphamide Metabolism: Impact on Pharmacokinetics and Antitumor Activity," <i>J. Pharmacol. Exp. Ther.</i> 288:928-937, The American Society for Pharmacology and Experimental Therapeutics (1999)			
	ES	ZON, G., "Cyclophosphamide Analogues" in <i>Progress in Medicinal Chemistry</i> , Ellis, G.P., <i>et al.</i> , eds., Elsevier Biomedical Press, Chapter 4, pp. 205-246 (1982)			
	ET	ZON, G., <i>et al.</i> , "NMR Spectroscopic Studies of Intermediary Metabolites of Cyclophosphamide. A Comprehensive Kinetic Analysis of the Interconversion of <i>cis</i> - and <i>trans</i> -4-Hydroxycyclophosphamide with Aldophosphamide and the Concomitant Partitioning of Aldophosphamide between Irreversible Fragmentation and Reversible Conjugation Pathways," <i>J. Med. Chem.</i> 27:466-485, American Chemical Society (1984)			
	EU	International Search Report for related International Application No. PCT/US03/34709, European Patent Office, Netherlands, mailed May 11, 2004			
	EV	Copy of Office Action for Co-pending United States Application No. 10/698,928, Boyer, S., <i>et al.</i> , filed October 31, 2003, mailed July 5, 2005			

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Examiner Signature		Date Considered	
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